a) forming a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2; and

b) randomly distributing a population of microspheres on said surface such that individual sites contain microspheres, wherein said population comprises at least a first and second subpopulation, wherein said first and second subpopulations each comprise:

i) a different protein bioactive agent; and

ii) a different nucleic acid identifier binding ligand;

c) binding a first and second distinct decoder binding ligand to said first and second distinct identifier binding ligand.

REMARKS

Claims 1-36 have been cancelled, claims 37-55 have been added. For the Examiner's convenience, a copy of the currently pending claims is appended hereto as Appendix A. A copy of the amendments showing changes made is also appended here to as Appendix B.

Claims 37-55 have been added to include clearer language. Support for the new claims may be found in the claims as originally filed.

Objections to Specification

The Examiner objected to the disclosure because the specification of a misspelling at page 9, line 2. The word "isery" should read "is very." The specification has been corrected to eliminate this clear error. Applicant thanks the Examiner for directing attention to this error.

35 U.S.C. § 112

Without admitting the propriety of the rejection, the claims have been cancelled, and new claims have been added. Accordingly, the rejection should be withdrawn.

35 U.S.C. § 102, Brenner et al.

Claims 1, 3, 7, 18, 20, 22, 25, and 27-36 were rejected under 35 U.S.C. § 102(e) as being anticipated by Brenner et al., U.S. Patent No. 5,863,722 (hereinafter "Brenner"). Although the rejected claims have been cancelled, the art cited by the Examiner is being addressed.

Brenner teaches a method of sorting polynucleotides with oligonucleotide tags. An aspect of the Brenner invention is the use of oligonucleotide tags for sorting polynucleotides by specifically hybridizing tags attached to the polynucleotides to their complements on solid phase supports.

The claims of the present application, on the other hand, are directed to array compositions and methods of making the array composition comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said discrete sites are wells. The invention comprises first and second subpopulations of microspheres , wherein the microspheres are randomly distributed on the sites.

As the Examiner is aware, "[i]t is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367 (Fed. Cir. 1986).As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference." See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1497 (Fed.Cir 1995).

Applicant submits that Brenner does not anticipate the presently pending claims. Regarding claims 37 and 51, Applicants submit that Brenner fails to disclose microspheres distributed in wells on a substrate wherein the wells (discrete sites) are at a density of at least 100 sites per 1 mm^2. Moreover, regarding claim 51, Brenner does not teach that the substrate is a fiber optic bundle.

Regarding claims 52, 54 and 55, Applicants submit that Brenner fails to disclose that different subpopulations of microspheres each include a different protein bioactive agent and a different nucleic acid identifier binding ligand. Moreover, regarding claim 54, Brenner does not teach that the substrate is a fiber optic bundle.

Accordingly, Brenner fails to teach each and every element of the presently pending claims. Therefore, Brenner does not anticipate the present invention; Applicants respectfully request the Examiner to withdraw the rejection.

35 U.S.C. § 102, Chelsky et al.

Claims 23, 24, and 28 were rejected under 35 U.S.C. § 102(e) as being anticipated by Chelsky et al., U.S. Patent No. 5,856,083 (hereinafter "Chelsky"). While these claims have been canceled herein, Applicants will address this art that was cited by the Examiner.

Chelsky is directed to a lawn assay for compounds that affect enzyme activity or bind to target molecules. The assay involves the steps of: providing an enzyme or target molecule, providing a plurality of beads, carrying out an enzymatic catalysis or binding of compounds to the target molecule in the colloidal matrix; and monitoring a photometrically detectable change in the substrate, a coenzyme, or enzyme cofactor involved in the enzymatic reaction, or in the labeled ligand to determine a zone of activity in the matrix associated with one or more of the compounds. The beads of Chelsky are screened when contacted with a colloidal matrix, such as agarose. The beads may be contacted with an enzyme contained in the agarose. Conversion of the substrate to product is measured by monitoring a photometric change in the substrate, or in a coenzyme or cofactor involved in the reaction.

The claims of the present application, on the other hand, are directed to array compositions and methods of making the array composition comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said discrete sites are wells. The invention comprises first and second subpopulations of microspheres , wherein the microspheres are randomly distributed on the sites.

Applicant submits that Chelsky does not anticipate the presently pending claims. Regarding claims 37 and 51, Applicants submit that Chelsky fails to disclose microspheres distributed in wells on a substrate wherein the wells (discrete sites) are at a density of at least 100 sites per 1 mm^2. Moreover, regarding claim 51, Chelsky does not teach that the substrate is a fiber optic bundle.

Regarding claims 52, 54 and 55, Applicants submit that Chelsky fails to disclose that different subpopulations of microspheres each include a different protein bioactive agent and a different nucleic acid identifier binding ligand. Moreover, regarding claim 54, Chelsky does not teach that the substrate is a fiber optic bundle. Finally, Chelsky also lacks a teaching of first and second distinct decoder binding ligands bound to said first and second distinct bioactive agents, respectively (claim 55).

Therefore, Chelsky does not anticipate every element of the present claims. Applicant therefore respectfully requests withdrawal of the rejection.

Provisional Double-Patenting Rejection

Claims 1-7 and 15-36 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 15-22, and 24 of copending application Serial No. 09/748,706.

In light of the amendment of the claims herein, Applicant submits that this rejection is moot. However, if the rejection is applied to the new claims as a provisional double patenting rejection, the Examiner is requested to resolve the remaining issues and give an indication of otherwise allowable subject matter with regard to one of the pending cases, per the guidance provided in M.P.E.P. §§ 804 and 822.01.

CONCLUSION

Applicant submits that the claims amended are ready for allowance and the Examiner is respectfully requested to provide early notification to this effect.

The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues remain.

Respectfully submitted,
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37. (New) An array composition comprising:

a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said discrete sites are wells; and

b) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label.

38. (New) An array according to claim 37, wherein each subpopulation further comprises a different identifier binding ligand.

39. (New) An array according to claim 37 or 38, further comprising at least one decoder binding ligand comprising a label.

40. (New) An array composition according to claim 37 wherein said bioactive agents are nucleic acids.

41. (New) An array composition according to claim 40 wherein said nucleic acids are DNA.

42. (New) An array composition according to claim 40 wherein said nucleic acids are single stranded nucleic acids.

43. (New) An array composition according to claim 40 wherein said nucleic acids are double stranded nucleic acids.

44. (New) An array composition according to claim 37 wherein said bioactive agents are proteins.

45. (New) An array composition according to claim 37 wherein said substrate is a fiber optic bundle.

46. (New) An array composition according to claim 37 wherein said substrate is glass.

47. (New) An array composition according to claim 37 wherein said substrate is plastic.

48. (New) An array composition according to claim 40, 41, 42, 43, 44, 45, 46 or 47, wherein each subpopulation further comprises a different identifier binding ligand.

49. (New) An array composition according to claim 48, further comprising at least one decoder binding ligand comprising a label.

50. (New) An array composition according to claim 49, wherein said label is a fluorophore.

51. (New) An array composition comprising:

a) a fiber optic substrate with a surface comprising wells at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres randomly distributed in said wells, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label.

52. (New) An array composition comprising:

a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first and said second subpopulations each comprise:

i) a different protein bioactive agent; and
ii) a different nucleic acid identifier binding ligand;

wherein said microspheres are randomly distributed on said sites.

53. (New) An array composition according to claim 15 wherein said substrate is selected from the group consisting of fiber optic bundles, plastic and glass.

54. (New) An array composition comprising:

a) a fiber optic bundle with a surface comprising discrete wells at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first and said second subpopulations each comprise:

        i) a different protein bioactive agent; and

        ii) a different nucleic acid identifier binding ligand;

wherein said microspheres are randomly distributed on said sites.

55. (New) A method of making a composition comprising:

    a) forming a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2; and

    b) randomly distributing a population of microspheres on said surface such that individual sites contain microspheres, wherein said population comprises at least a first and second subpopulation, wherein said first and second subpopulations each comprise:

        i) a different protein bioactive agent; and

        ii) a different nucleic acid identifier binding ligand;

    c) binding a first and second distinct decoder binding ligand to said first and second distinct identifier binding ligand.

IN THE SPECIFICATION

The paragraph beginning at page 8, line 31, has been amended as follows:

By "substrate" or "solid support" or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates [isery] is very large. Possible substrates include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon[J]®, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, optical fiber bundles, and a variety of other polymers. In general, the substrates allow optical detection and do not themselves appreciably fluorescese.

IN THE CLAIMS

Claims 1-36 are canceled.

Please add the following new claims:

- -37. (New) An array composition comprising:

a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2, wherein said discrete sites are wells; and

b) a population of microspheres randomly distributed on said sites, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label.

38. (New) An array according to claim 37, wherein each subpopulation further comprises a different identifier binding ligand.

39. (New) An array according to claim 37 or 38, further comprising at least one decoder binding ligand comprising a label.

40. (New) An array composition according to claim 37 wherein said bioactive agents are nucleic acids.

41. (New) An array composition according to claim 40 wherein said nucleic acids are DNA.

42. (New) An array composition according to claim 40 wherein said nucleic acids are single stranded nucleic acids.

43. (New) An array composition according to claim 40 wherein said nucleic acids are double stranded nucleic acids.

44. (New) An array composition according to claim 37 wherein said bioactive agents are proteins.

45. (New) An array composition according to claim 37 wherein said substrate is a fiber optic bundle.

46. (New) An array composition according to claim 37 wherein said substrate is glass.

47. (New) An array composition according to claim 37 wherein said substrate is plastic.

48. (New) An array composition according to claim 40, 41, 42, 43, 44, 45, 46 or 47, wherein each subpopulation further comprises a different identifier binding ligand.

49. (New) An array composition according to claim 48, further comprising at least one decoder binding ligand comprising a label.

50. (New) An array composition according to claim 49, wherein said label is a fluorophore.

51. (New) An array composition comprising:

a) a fiber optic substrate with a surface comprising wells at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres randomly distributed in said wells, wherein said population comprises at least a first and a second subpopulation each comprising a different bioactive agent and do not comprise a label.

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52. (New) An array composition comprising:

a) a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first and said second subpopulations each comprise:

i) a different protein bioactive agent; and

ii) a different nucleic acid identifier binding ligand;

wherein said microspheres are randomly distributed on said sites.

53. (New) An array composition according to claim 15 wherein said substrate is selected from the group consisting of fiber optic bundles, plastic and glass.

54. (New) An array composition comprising:

a) a fiber optic bundle with a surface comprising discrete wells at a density of at least 100 sites per 1 mm^2; and

b) a population of microspheres comprising at least a first and a second subpopulation, wherein said first and said second subpopulations each comprise:

i) a different protein bioactive agent; and

ii) a different nucleic acid identifier binding ligand;

wherein said microspheres are randomly distributed on said sites.

55. (New) A method of making a composition comprising:

a) forming a substrate with a surface comprising discrete sites at a density of at least 100 sites per 1 mm^2; and

b) randomly distributing a population of microspheres on said surface such that individual sites contain microspheres, wherein said population comprises at least a first and second subpopulation, wherein said first and second subpopulations each comprise:

i) a different protein bioactive agent; and

ii) a different nucleic acid identifier binding ligand;

c) binding a first and second distinct decoder binding ligand to said first and second distinct identifier binding ligand.- -.